Non-toxic, isoform-specific histone deacetylase inhibitors as a therapeutic for the treatment of cancer and neurodegenerative diseases

Technology #cu14072

Histone deacetylases (HDAC) are a class of enzymes, responsible for regulating gene expression. Aberrant HDAC activity has been implicated in a variety of diseases including cancer and neurodegenerative disorders. This technology includes a novel set of compounds that can specifically inhibit HDAC6. HDAC inhibitors have shown substantive promise as an anticancer agent, and there is mounting evidence to support its utility in neurodegenerative disease treatment. The Industry has experienced limited success in developing isoform specific HDAC inhibitors, resulting in concerns related to off-target toxicities. The high selectivity and low toxicity of these HDAC6-specific compounds make them promising candidates for drug development in cancer and neurodegenerative diseases.

Highly selective compounds show improved toxicity profiles

HDACs are enzymes that deacetylate lysine residues from histones, a modification that suppresses the expression of certain genes. Thus, aberrant activity of HDACs leads to transcription misregulation, contributing to disease development. In collaboration with Dr. Paul Marks at Memorial Sloan Kettering, Dr. Ron Breslow from Columbia University's Department of Chemistry has developed a series of compounds that specifically inhibit HDAC6, providing significant advantage for drug development due to its decreased toxicity. HDAC6 is known to deacetylate proteins such as tubulin and chaperone protein HSP90, as well as directing misfolded proteins to aggresomes for degradation. Thus, with HDAC6 playing multiple roles in regulating cellular function, such as axonal transport and protein degradation, the HDAC6 inhibitors included in this technology show great potential as a therapeutic to treat either cancer or a large variety of neurodegenerative diseases that involve long neuronal transport and misfolded protein aggregation.

These compounds have been well-characterized in mouse models and have demonstrated cooperative effects in combination with other anticancer agents.

Lead Inventor:

Ronald Breslow, Ph.D.

Applications:

- Therapeutic for cancer treatment
- Combination therapy with other anticancer agents
- Therapeutic for Alzheimer’s disease
- Therapeutic for Parkinson’s disease
- Therapeutic for ALS
- Therapeutic for any neurodegenerative disorder involving aberrant protein degradation and axonal transport
- Research tool to study HDACs in disease models

Advantages:
- High selectivity
- Low toxicity
- Cooperative effects in combination with other cancer agents
- Well-characterized compounds in animal models, reducing time and cost of developing therapeutics

Patent Information:
Patents Pending WO/2015/100363 ; WO/2013/052110

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Related Publications:


Inventors

Ronald Breslow